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UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	:	**October 21, 2001**
LISZIEWICZ, et al.	:	**Atty Docket No. RGT 9771**
10/081,922 *DIVISION OF* Serial No. 09/153,198	:	**Group 1632**
Filed: 15 September 1998	:	**Examiner: Wilson**

For: Method of Delivering Genes into Antigen Presenting Cells of the Skin

Commissioner for Patents
And Trademarks
Washington, D.C. 20231

Phone (571) 272-0738 FAX (703) 872-9306[1]

SPECIAL PROCEDURES SUBMISSION

The Applicants respectfully request a meeting with the Practice Specialist, the Supervisory Examiner, and the Examiner in the referenced case. The enclosed Final Rejection is not responsive to the enclosed Amendment.

Enclosed are 1) an office action bearing a mail date of 09/22/04, an Amendment filed 06/07/04, an extra copy of the amended Claims filed 06/24/04 and parent patent USPN 6,420,176. The present application is a Division of the enclosed patent. Among other things, the Examiner has maintained ***new matter*** rejections over the parent, despite being shown where the exact wording is found in the parent patent as published, or cited in the original claims as filed. For example, the Examiner has objected to the genus "Antigen Presenting Cells"which is found in the title of the parent patent, and "mixtures thereof" found in original claim 8.

Respectfully Submitted,

Valerie E. Looper

Valerie E. Looper
Registration No. 33,007

The Law Offices of
Valerie E. Looper
11726 Lightfall Court
Columbia, Maryland 21044
Telephone: (410) 715 - 5771
fax: (410) 715-5773

[1] This letter is being forwarded to the USPTO, 2001 S. Clark Place Customer Window, Crystal Plaza Two, Lobby, RM 1B03, Arlington, VA 22202 via courier by Valerie E. Looper on October 21, 2004, signed Valerie E. Looper

Application No.	Applicant(s)	
10/081,922	LISZIEWICZ ET AL.	
Examiner	**Art Unit**	
Michael C. Wilson	1632	

Office Action Summary

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33,35 and 37-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33,35 and 37-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 6-7-04 was non-responsive because it was in the wrong format – a complete listing of all the claims was not present. The amendment filed 6-24-04 has been entered.

Claims 1-22, 34 and 36 have been canceled. Claim 42 has been added. Claims 23-33, 35 and 37-42 are under consideration.

Applicant's arguments filed 6-7-04 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

This application repeats a substantial portion of prior Application No. 09/153198, filed 9-15-98, and adds and claims additional disclosure not presented in the prior application. Specifically, the preliminary amendment filed with the instant application added claim 23, which required mixing DNA and "a compound selected from the group consisting of sugars, polyethylenimine, polyethylenimine derivatives, and mixtures thereof". Neither 09/153,198 nor the instant disclosure provides support for "mixtures thereof" in this context. While the amendment filed 2-21-02 states claims 23-41 are supported by the original claims, the originally claims do not provide support for combining mixtures of sugar, polyethylenimine and polyethylenimine derivatives, with DNA. Therefore, this application is a continuation-in-part of the prior application and not

a "division" as currently described by applicants in the first line of the specification. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

Claims 23-33, 35 and 37-41 (methods of transuding cells and methods of inducing an immune response in mammals) are patentably distinct invention from the claims in parent application 09/153,198, now US Patent 6,240,176, filed 9-15-98 (products).

Specification

The amendment to the first line of the specification filed 6-7-04 has omitted original text, i.e. reference to "USSN 09/153,198" has been deleted completely without being marked as being deleted. The correct format for the first line is as follows: "This application is a division of US Application 09/153,198, filed 9-15-98, now US Patent 6,420,176, which is a continuation-in-part of...." It is noted that the instant application appears to be a CIP and not a DIV of '198.

The status of applications on pg 17, line 34-38, have been updated.

The status of the application on pg 13, line 36, will need updated as necessary.

The status of the application on pg 18, line 32, will need updated as necessary.

The amendment filed 2-21-02 remains objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the sentence added to

the paragraph on pg 13, line 26, does not have support in the specification as originally filed. Applicant is required to cancel the new matter in the reply to this Office Action. Applicants have not addressed this issue.

Claim Objections

The objection of claims 28-30 because they have parenthetical reference to pages of the specification has been withdrawn in view of the amendment.

Claim 35 is objected to. The phrase "steps from the group consisting of receptor stimulation, toxin activation, or tissue or cell injury" is not in proper Markush format and can be clarified. The phrase should be –steps selected from the group consisting of receptor stimulation, toxin activation, tissue injury, and cell injury."

Claim Rejections - 35 USC ' 112

1. Claims 23-33, 35 and 37-41 remain rejected and claim 42 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

The genus of antigen presenting cells (APCs) in claim 23 is new matter. The specification as originally did non contemplate transducing any APCs other than dendritic cells. Applicants argue the phrase is found in the title and abstract of parent application 09/153,198 (US Patent 6,420,176); therefore, applicants conclude the

phrase is not new matter. Applicants' argument is not persuasive. The instant application appears to be a continuation-in-part and not a divisional of 09/153,198 (US Patent 6,420,176) (see explanation above). Please provide support for transfecting antigen presenting cells with a gene delivery complex by applying the complex to the skin or mucosa as claimed using the instant application.

The phrase "mixtures thereof" (claim 23) is considered new matter. The specification does not contemplate combining PEI with derivatives of PEI or combining different derivatives of PEI. It is noted that claim 8 as originally filed stated "wherein the complex is selected from the group consisting of DNA conjugates of sugars, polyethylenimine, polyethylenimine derivatives, and mixtures thereof"; however, the claim was rejected under indefiniteness because it could not be determined what the phrase meant (see first office action in parent application). Because of the indefiniteness of the claim as originally filed, it is not readily apparent that the phrase was intended to encompass mixing PEI with PEI derivatives or mixing different PEI derivatives as encompassed by the claims as amended. Therefore, the specification as originally filed did not support mixing PEI with PEI derivatives or different PEI derivatives.

Applicants argue claim 8 as originally filed supports "mixtures thereof" because it states, "wherein the complex is selected from the group consisting of DNA conjugates of sugars, polyethylenimine, polyethylenimine derivatives, and mixtures thereof". Applicants' argument is not persuasive. It is not readily apparent that the phrase in claim 8 was intended to mean that sugars, polyethylenimine and polyethylenimine

derivatives were mixed and then "conjugated" with DNA. As written, claim 8 appears to be limited to a complex comprising a mixture of DNA conjugates. Claim 8 does not teach or suggest selecting a complex comprising DNA and a mixture of sugars, polyethylenimine or polyethylenimine derivatives, as newly claimed. The scope of a complex comprising a mixture of DNA conjugates (claim 8) is different than the scope of a complex comprising DNA and a mixture of sugars, polyethylenimine and polyethylenimine derivatives (claim 23).

Applicants argue Examples 6, 7 and 10 support "mixtures thereof" in claim 23 because they teach combining DNA and glucose and DNA and PEI in a glucose solution. Applicants' argument is not persuasive. The examples do not teach combining DNA and glucose with DNA and PEI. The examples do not teach DNA and PEI in glucose solution. Example 6 uses DNA conjugated with PEI-mannose, PEI-galactose or PEI-glucose. Example 6 does not combine DNA with a mixture of PEI-mannose, PEI-galactose and/or PEI-glucose. Example 6 does not combine the PEI derivates with glucose. Example 7 uses DNA conjugated with PEI-mannose. Example 7 does not combine PEI-mannose with glucose, any sugar or any other PEI derivatives. Example 10 is a sugar-DNA complex without PEI and does not combine the complex with other sugars PEI, or PEI derivatives.

Claim 23 remains rejected under new matter because no support for the breadth of the claim has been provided. The specification as originally filed did not teach or suggest "transducing APCs of the skin" in any "animal" by applying the complex to the "skin or mucosa surfaces" as broadly claimed.

Applicants point to original claim 19 which is directed toward immunizing animals against viral infection using a gene delivery complex of any one of claims 1-10 by "exposing the animal to the gene delivery complex described in Claim 17 on the skin or on mucosa surfaces." Claim 19 does not contemplate transducing APCs by applying the complex to the skin or mucosa as currently required in claim 23. In addition, skin or mucosal delivery of a gene delivery complex as in original claim 19 is limited to preventing or treating reverse-transcriptase-dependent virus infection, which is much narrower in scope than transfecting APCs in any animal using DNA encoding any immunogenic protein as in claim 23. It is not readily apparent that the specification could be pieced together to come up with the combination of elements claimed. It is not readily apparent that applicants contemplated transducing any APCs with DNA encoding any immunogenic protein by administering a complex to the skin or mucosa as broadly claimed.

Claim 25 remains rejected under new matter because the specification as originally filed did not contemplate the genus of "polyethylenimine derivates that target a receptor found on the surface of antigen presenting cells". The only such PEI described in the specification that targets the mannose receptor is mannosylated PEI as in claim 26, which is not adequate representation of the genus of "polyethylenimine derivates" that target a receptor found on the surface of antigen presenting cells".

Applicants argue support for "polyethylenemine derivatives" is in claim 8 as originally filed. Applicants' argument is not persuasive because the rejection is based on the genus of "polyethylenimine derivates" that have a particular function, i.e. that

target a receptor found on the surface of APCs. Mannosylated PEI does not represent the genus of polyethylenemine derivatives in claim 25. Please use the instant application for providing support for claims in the instant application because the instant application may be a CIP and not a DIV of the parent application.

Claim 27 remains new matter because support for a mannosylated PEI "derived from a linear PEI 22 kDA" cannot be found. Applicants argue support can be found in col. 10, line 41 of parent application. Applicants' argument is not persuasive. The citation cannot be found. Please use the instant application for providing support for claims in the instant application because the instant application may be a CIP and not a DIV of the parent application. Example 6 does not teach PEI-glucose or PEI-galactose targeted the mannose receptor.

Support for "electrostatically neutral" in claim 28 can be found on pg 22, lines 3-8.

The phrase "3:1-10:1 molar equivalents" (claim 29) remains new matter. Pg 22, lines 9-16, only contemplate 5:1, 3:1 and 10:1 ratios. It is not readily apparent that the range 3:1 to 10:1 was contemplated.

The limitation of "5:1 molar equivalents" (claim 30) has support on pg 22, line 11.

The rejection regarding the phrase "about 5-10" (claim 32) and "about 8" (claim 33) has been withdrawn because the term "about" has been deleted.

The rejection regarding activating the APCs of the skin or mucosa in claim 34 as being new matter has been withdrawn because the claim has been canceled.

The rejection regarding applying the complex to the skin or mucosa and further obtaining receptor stimulation, toxin activation, or tissue or cell injury in claim 35 has been withdrawn because support has been found on pg 16, lines 32-38.

The rejection regarding proteins "derived" from a reverse-transcriptase dependent virus in claim 36 has been withdrawn because the claim has been cancelled.

New claim 42 is new matter because pg 22, lines 9-16, taught the ratio of 3:1 was not used in the method of the invention ("in contrast to 3:1 (N:P) PEI-DNA complex").

2. Claims 23-33, 35 and 37-41 remain rejected and claim 42 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention for reasons of record.

The claims are drawn to transfecting antigen presenting cells (APCs) by applying a complex to the skin or mucosa of an animal, wherein the complex comprises i) DNA encoding an immunogenic protein from a lentivirus and ii) sugar, polyethylenimine (PEI), a PEI derivative, or mixture thereof.

The specification suggests using the method claimed to induce an immune response in a mammal (pg 20, Example 4). However, merely inducing an immune response in a mammal, in and of itself, does not have a use by itself because inducing an immune response is only described in the specification as being used to obtain a

therapeutic or prophylactic effect (pg 2, lines 20-24; pg 18, lines 2-8). Therefore, inducing an immune response according to the specification must result in a therapeutic or prophylactic effect to have an enabled use. The methods using DNA encoding an immunogenic protein as claimed lack written description because the specification does not provide adequately describe how to induce a therapeutic or prophylactic immune response using the method claimed.

Applicants argue the analysis of the claims by the examiner is in error because the claims merely require transfecting APCs and do not require a step in which therapy or prophylaxis is obtained. Applicants' argument is not persuasive. The claims must be read in light of the specification. The only purpose for applying DNA encoding a protein from a lentivirus to the skin or mucosa of an animal is for therapy or prophylaxis. Therefore, it is reasonable to determine whether applicants have adequately described to those skilled in the art the steps required to applying DNA encoding a protein from a lentivirus to the skin or mucosa of an animal and obtain therapy or prophylaxis despite the fact that the claims do not expressly require obtaining therapy or prophylaxis.

The genus of transfecting any antigen presenting cell (APCs) in claim 23 lacks written description. The specification as originally did not contemplate transfecting any APCs other than dendritic cells. The species of dendritic cells is not adequate to support the genus of APCs.

Claims 23 and 37-39 require using DNA encoding a protein from a lentivirus (23), specifically an HIV virus (37), more specifically from a replication-defective HIV virus (38), more specifically an integration-defective, replication-defective HIV virus (39). The

specification does not enable one of skill to use DNA encoding a lentiviral protein transfect APCs and treat or prevent disease. Applicants describe using plasmids encoding replication-defective, integrase-defective retroviral DNA in related application 08/989,301 as being non-lethal and capable of inducing a therapeutic/prophylactic immune response when administered in vivo. However, Adachi (J. Virol., Aug. 1986, Vol. 59, pg 284-291) taught such viruses were still infectious. DNA encoding a lentiviral protein, specifically DNA encoding a "replication defective retroviral" protein that is non-lethal and capable of inducing a therapeutic/prophylactic immune response, is not adequately described by applicants. Nowhere have applicants provided any evidence that the amount of expression of viral protein is adequate to induce a therapeutic/prophylactic immune response or that the virus does not replicate too much and cause disease. Use of the plasmids encoding replication-defective retrovirus in animals as claimed would not treat or prevent disease because the virus would replicate and cause disease. Applicants appear to be attempting to find DNA comprising a lentiviral protein that expresses adequate viral protein such that a cellular immune response can be obtained, wherein said DNA i) does not make retroviral particles or ii) does make viral particles that replicate to a low degree without causing disease. Naming a type of material that may exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming a method of using DNA encoding replication-defective retroviral proteins without defining the DNA that will encode adequate amounts of retroviral protein to induce a therapeutic/prophylactic effect without causing retroviral particle formation or retroviral

infection is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

Applicants argue the examiner has mischaracterized claims 36-39. Applicants believe the examiner's discussion of retroviruses is misplaced because retroviruses have RNA while the instant claims require DNA. Applicants' argument is wholly unfounded. While retroviral particles have RNA, retroviral DNA is used to transfect packaging cells and make the retroviral particles comprising RNA. The specification describes using constructs comprising DNA encoding replication or integration defective HIV (pg 13, lines 26-30). Therefore, the DNA in the claims 36-39 can be transcribed into RNA and made into retroviral particles upon division of the transfected cell. As such, it is reasonable to conclude that claim 23 encompasses transfecting APCs in an animal with DNA encoding lentiviral proteins resulting in lentiviral particle formation (comprising RNA) and lentiviral infection, wherein the protein induces an immune response but the retroviral particles do not replicate too much and cause disease. This DNA encompassed by claim 23 and described vaguely by applicants lacks written description for reasons above because the structure having the function has not been described.

The phrase "PEI, PEI derivatives and mixtures thereof" in claim 23 lacks written description. The specification does not contemplate combining PEI with derivatives of

PEI or combining different derivatives of PEI. It is not readily apparent that applicants were in possession or even contemplated any "mixture thereof" as broadly claimed.

Applicants argue claim 8 as originally filed supports "mixtures thereof" because it states "wherein the complex is selected from the group consisting of DNA conjugates of sugars, polyethylenimine, polyethylenimine derivatives, and mixtures thereof". Applicants' argument is not persuasive. It is not readily apparent that the phrase in claim 8 was intended to mean that sugars, polyethylenimine and polyethylenimine derivatives were mixed and then "conjugated" with DNA. As written, claim 8 appears to be limited to a complex comprising a mixture of DNA conjugates. Claim 8 does not teach or suggest selecting a complex comprising DNA and a mixture of sugars, polyethylenimine or polyethylenimine derivatives, as newly claimed. The scope of a complex comprising a mixture of DNA conjugates (claim 8) is different than the scope of a complex comprising DNA and a mixture of sugars, polyethylenimine and polyethylenimine derivatives (claim 23). Applicants argue Example 6 supports "mixtures thereof" in claim 23 because they teach combining DNA and glucose and DNA and PEI in a glucose solution. Applicants' argument is not persuasive. Example 6 does not teach combining DNA and glucose with DNA and PEI or combining DNA and PEI in glucose solution. Example 6 uses DNA conjugated with PEI-mannose, PEI-galactose or PEI-glucose. Example 6 does not combine DNA with a mixture of PEI-mannose, PEI-galactose and/or PEI-glucose. Example 6 does not combine the PEI derivates with glucose.

3. Claims 23-33, 35 and 37-41 remain rejected and claim 42 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record.

Claim 23 is directed to transducing antigen presenting cells (APCs) by applying a complex to the skin or mucosa of an animal, wherein the complex comprises i) DNA encoding a an immunogenic protein from a lentivirus and ii) sugar, polyethylenimine (PEI), a PEI derivative, or mixture thereof.

The specification describes using the method claimed to induce an immune response in a mammal (pg 20, Example 4). However, merely inducing an immune response in a mammal, in and of itself, does not have an enabled use by law because inducing an immune response is only described in the specification as being used to obtain a therapeutic or prophylactic effect (pg 2, lines 20-24; pg 18, lines 2-8). Therefore, inducing an immune response according to the specification must result in a therapeutic or prophylactic effect to have an enabled use. The ordinary artisan reading the claimed invention in view of the specification would only determine that the method claimed was for the purpose of therapy or prophylaxis. Applying DNA encoding an immunogenic lentiviral protein to an animal as claimed is not enabled because the specification does not provide adeqaute guidance for one of skill to induce a therapeutic or prophylactic immune response using the method claimed.

Klatzmann and Sticker taught retroviral vaccines have been unable to protect against infection (Klatzmann, US Patent 6,140,114, Oct. 31, 2000; Stricker et al., Medical Hypotheses, June 1997, Vol. 48, pg 527-9). Overall, a lack of understanding about protective immunity to retroviruses such as HIV, the sequence variability and the rapid replication of retroviruses contribute the ineffectiveness of vaccines against retroviruses (Bangham, Nov. 29, 1997, Lancet, Vol. 350, pg 1617-1621; pg 1617, top of col. 1).

The specification teaches making plasmids encoding replication defective, integrase-defective HIV as described in application 08/989,301 (pg 18, line 30-32). In application 08/939,301, applicants call such retroviruses "Class 4" viruses which are infectious but replication-defective (pg 15, lines 1-5). In application 08/989301, applicants teach that replication defective HIV that does not replicate effectively is inadequate to elicit a protective cellular immune response. Alternatively, replication defective HIV that does replicate effectively causes disease and sometimes fatal (pg 3, line 17 through pg 4, line 3). The amount of replication of a retrovirus required to obtain a therapeutic cellular immune response without causing disease was unknown in the art at the time of filing. It was also unknown how to make a retrovirus with the adequate amount of replication that would provide an adequate cellular immune response without causing disease. Without being able to make such a retrovirus, it was unknown how to use such a virus to obtain a therapeutic or prophylactic cellular immune response in a host.

The specification does not provide adequate guidance regarding how to obtain a therapeutic or prophylactic effect by applying a replication defective retrovirus in an animal as claimed. The specification does not teach the amount of a cellular immune response that is therapeutic or prophylactic effect against a replication defective retrovirus. The amount of dendritic cells required to obtain adequate antigen presentation is not provided in the specification. The amount of retroviral protein expression required to obtain the desired cellular immune response is not provided in the specification. The amount of replication and infectiousness required to obtain the desired balance between therapy and pathogenicity is not provided in the specification. Given the teachings in the specification taken with the unpredictability in the art at the time of filing, it would have required one of skill in the art at the time of filing undue experimentation to determine how to make and/or use a replication defective retrovirus to obtain a therapeutic/prophylactic effect without causing disease or death.

In addition, it was unpredictable what vector, promoter, dosage, cells, level of expression and route of administration would provide a therapeutic or prophylactic effect using *in vivo* or *ex vivo* gene therapy (Miller 1995, FASEB J., Vol. 9, pg 190-199; pg 198, col. 1; Deonarain, 1998, Expert Opin. Ther. Pat., Vol. 8, pg 53-69; pg 53, 1st ¶, pg 65, 1st ¶ under Conclusion section; Verma, Sept. 1997, Nature, Vol. 389, pg 239-242; see entire article, specifically pg 240, sentence bridging col. 2 and 3; Crystal, 1995, Science, Vol. 270, pg 404-410, pg 409; Ross, Sept. 1996, Human Gene Therapy, Vol. 7, pg 1781-1790; pg 1782, col. 2, 1st full ¶; pg 1789, col. 1, 1st ¶).

The specification does not enable applying DNA encoding a lentiviral protein to the skin or mucosa to transfect APCs and obtain a therapuetic or prophylactic effect. The specification does not teach applying DNA to the mucosa results transfection of APCs or in expression of the protein in the APCs. The specification does not teach the amount of lentiviral protein expression required for the APCs to present adequate antigens to the immune system such that a therapuetic/prophylactic immune response is obtained. The specification does not teach the immune response to a lentiviral antigen required to treat or prevent disease. The specification does not provide the combination of vector, promoter, dosage, level of expression that would result in a therapeutic/prophylactic effect. Given the teachings in the specification taken with the unpredictability in the art at the time of filing, it would have required one of skill in the art at the time of filing undue experimentation to determine the vector, promoter, cell, dosage, level of expression and route of administration required to obtain a therapeutic or prophylactic effect using the method claimed.

Applicants argue the analysis of the claims by the examiner is in error because the claims merely require transfecting APCs and do not require a step in which therapy or prophylaxis is obtained. Applicants' argument is not persuasive. The claims must be read in light of the specification. The only purpose for applying DNA encoding a lentiviral protein to the skin or mucosa of an animal is for therapy or prophylaxis. Therefore, it is reasonable to determine whether applicants have provided adequate guidance for the sole disclosed use, i.e. whether applicants provide adequate guidance for those skilled in the art to apply DNA encoding a protein from a lentivirus to the skin

or mucosa of an animal and obtain therapy or prophylaxis. Merely transfecting APCs with DNA encoding a lentiviral protein as in claim 23 has no meaning without obtaining therapy or prophylaxis.

Applicants argue a CTL response *in vitro* was obtained; therefore, applicants conclude the method can be used to obtain a therapuetic or prophylactic effect in vivo. Applicants' argument is not persuasive. First, any declarations filed in parent applications will have to be filed in the instant applictition to be considered. Second, the immune response required to treat or prevent lentiviral infection was not know (see references of record above). For example, HIV patients have a CTL response to the HIV virus that is not therapeutic or prophylactic. The art was and continues to be completely absence of methods to treat or prevent lentiviral infection in vivo using by inducing an immune response. Evidence of a CTL response in vitro does not overcome such unpredictability in vivo. Applicants have not provided any evidence in this case (or any other) that showed obtaining an immune response in vivo, specifically a therapeutic or prophylactic immune response. Applicants have not provided any evidence that DNA expressed in vivo was adequately expressed to induce an immune response. Applicants have not provided any evidence that inducing a CTL response in vivo against a lentiviral protein is therapeutic or prophylactic in view of the overwhelming evidence to the contrary. The examiner is not requiring a showing or exemplification of inducing a therapuetic or prophylactic immune response using the method claimed; rather, the examiner is requiring a showing or exemplification of inducing a therapuetic or prophylactic immune response using the method claimed or a reasonable teaching of

the amount and type of protein to be expressed, the combination of promoter, protein and vector required to obtain adequate amounts of protein expression upon being applied to the skin or mucosa, how to adequately target the proper number of APCs by applying DNA to the skin or mucosa, the proper number of APCs to be targeted and the immune response required to treat or prevent lentiviral infection. In this case, applicants have provided neither a showing or a reasonable correlation.

3. Claims 23-33, 35 and 37-41 remain rejected and claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

Claim 23 remains indefinite because it is unclear whether "mixtures thereof" refers to mixtures of sugars, PEI and PEI derivatives or to mixtures of DNA with sugars, PEI or PEI derivatives. Applicants have not addressed this rejection.

The rejection of claim 23 as being indefinite because the preamble requires transducing APCs of the skin, but the body of the claim merely requires applying a complex to the skin/mucosa of an animal, has been withdrawn because the phrase "of the skin" has been deleted from the preamble of claim 23.

Claim 23 remains indefinite because as newly amended the complex is applied to the skin or mucosa surface of an animal but the preamble requires transduction of APCs. The body of the claim never obtains transfection of APCs or expression of the protein in APCs. Applicants' discussion of the parent application and the issued US

Patent is misplaced. Please use the instant application for clarifying the claims in the instant application because the instant application may be a CIP and not a DIV of the parent application.

Claim 23 as newly amended is indefinite because it is unclear if "transfection" is limited to transfection with plasmid or if the term encompasses infection with a viral particle. The specification does not define "transfection".

Claim 23 remains indefinite because the metes and bounds of what applicants consider "applying" to the skin cannot be determined. It is unclear if the phrase is limited to putting the complex on the skin or if the phrase encompasses subcutaneous injection which results in delivery of the complex under the skin. It is unclear if intravenous injection is encompassed by the phrase because such an injection does require contact of the complex to the skin when the injection passes through the skin. Applicants argue the claim excludes injections because they force fluid into a passage while "apply" is defined as to place in contact with, to lay or spread on. Applicants argument is not persuasive because subcutaneous injection results in the liquid going directly under the epidermis, i.e. the liquid is "in contact" with the skin.

Claim 27 remains indefinite as newly amended because it is unclear what applicants consider a mannosylated PEI from a PEI 22kDa. The phrase "a PEI 22kDA" is confusing because it is unclear if the PEI is 22kDa in weight or if PEI 22 kDa refers to some particular type of PEI. Applicants state the claim has been amended along the lines suggested by the Examiner, but the examiner did not suggest any amendment. Applicants have not addressed this issue.

Claim 29 remains indefinite because the phrases "3:1-10:1 molar equivalent of either polyethylenimine or polyethylenimine derivative amine per molar equivalent of DNA phosphate" is unclear. Page 22, lines 9-16, teaches that at the 5:1 (N:P) ratio, PEI-man-DNA is neutral. The specification states that N and P stand for nitrogen and phosphorus. The metes and bounds of the phrase also cannot be determined because it is unclear what applicants consider "molar equivalents" of N and P. The phrase "polyethylenimine or polyethylenimine derivative amine" is unclear because it is unclear if the phrase means 1) polyethylenimine or 2) polyethylenimine derivative amine or if the phrase means 1) polyethylenimine amine or polyethylenimine derivative amine.

Claim 30 remains indefinite because the phrase and "method of claim 29, wherein the complex comprises 5:1 molar equivalent of polyethylenemine derivative amine per molecular equivalent of DNA phosphate" is unclear. It is unclear if claim 30 is attempting to limit the range of 3:1-10:1 to a ratio of 5:1 or if claim 30 is attempting to limit the ratio to 5:1 and the type of amine to a polyethylenimine derivative amine. If applicants are just attempting to limit the range of 3:1-10:1 to 5:1, claim 30 should read the same as claim 29 except that "3:1-10:1" should be replaced with –5:1–. Applicants state the claim has been amended along the lines suggested by the Examiner, but the examiner did not suggest any amendment. Applicants have not properly addressed this issue.

Claim 31 remains indefinite because it is unclear whether the phrase "is formulated in a glucose solution" is limited to adding PEI, PEI-glu, PEI-gal, or PEI-man to a solution of glucose + water or if the phrase encompasses PEI-glu, PEI-gal, or PEI-

man + water. The specification teaches PEI may be glycosylated (pg 21, Table 1) or solubilized in glucose (pg 22, line 35). Overall, it is unclear whether the phrase is limited to PEI or PEI derivative added to glucose + water or if if the phrase encompasses adding PEI-glu to water to make a "glucose solution." Applicants' arguments are noted but do not address the issue.

Claims 32 and 33 are indefinite because the metes and bounds of the phrase "5-10% glucose" and "8% glucose" cannot be determined. The specification does not teach how to determine the units of the 5-10% glucose described on page 22, line 35-36. Thus, the metes and bounds of the claims cannot be determined. Applicants state the claims have been amended along the lines suggested by the Examiner, but the examiner did not suggest any amendment. Applicants have not addressed these issues.

The phrase "activating the antigen presenting cells" in claim 34 is indefinite. It is unclear if the phrase is further limiting what happens when the complex is "applied" as in claim 23 or if it is a step that is separate from "applying" the complex that occurs before or after "applying" the complex. It is unclear if "activation" refers to expression of the immunogenic protein in the context of an MHC molecule or to a second, separate step that causes "activation" of the APCs, e.g. applying an interleukin that causes APC activation.

The rejection regarding the metes and bounds of what applicants consider "activating" APCs in claim 35 has been withdrawn because the phrase "wherein the activating step" has been deleted.

The rejection regarding the metes and bounds of proteins "derived" has been withdrawn because none of the claims use the term.

The rejection regarding the metes and bounds of what applicants consider a "reverse transcriptase dependent virus" (claims 36 and 37) has been withdrawn because claim 36 has been cancelled and the phrase has been deleted from claim 37.

Claim Rejections - 35 USC ' 102

Claims 23-32, 35, 40 and 41 as newly amended remain rejected under 35 U.S.C. 102(e) as being anticipated by Behr (US Patent 6,013,240, Jan. 11, 2000; 102(e) date=2-28-97) as supported by Carson (US Patent 5,679,647).

Parent application 60/058,933 did not describe complexing DNA with a compound selected from the group consisting of sugars, PEI, PEI derivatives, or mixtures thereof (claim 23). Therefore, claim 23 does not get priority back to parent application 60/038,933 (filed 9-15-97). Parent application 09/153,198 (filed 9-15-98) described complexing DNA with PEI-mannose in a 5-10% glucose solution on pg 26, lines 1-9. Therefore, claims 23-33, 35 and 37-42 have priority to 9-15-98.

Behr taught a complex comprising i) PEI, and ii) plasmid DNA comprising a nucleic acid sequence encoding luciferase operatively linked to a promoter suspended in 5% glucose (col. 12, lines 53-57). Luciferase is an immunogenic protein because it is foreign to mammals and induces an immune response in mammals. Behr taught administering the complex to the skin or mucosa of an animal (claim 33, col. 6, lines 1-

19). Behr taught the DNA could encode an HIV peptide (col. 3, lines 57-67). The phrase "transfecting antigen presenting cells" in the preamble does not bear patentable weight in considering the art because it may not occur. However, the method of Behr inherently results in transfecting APCs because dendritic cells (a type of antigen presenting cell) are found in the epidermis (see definition of "dendritic cell", item 3).

While not relied upon for the basis of the rejection, Carson provides evidence that one of ordinary skill in the art would have had a reasonable expectation of successfully administering the DNA to the skin and transfecting APCs (col. 36-37, Examples 11-12). Therefore, one of ordinary skill in the art at the time of filing would have had a reasonable expectation of successfully taking the teachings of Behr and transfecting APCs of the skin.

Claims 25-27 are included because they are not limited to a compound that is mannosylated PEI or PEI "from a PEI 22 kDA;" claims 25-27 encompass glucose as in parent claim 24.

Claims 28-30 are included because Behr taught that between 5-20 equivalents of PEI amines are used relative to DNA phosphates (col. 8, lines 15-19), specifically 9 equivalents (col. 12, line 58). The instant specification teaches that such ratios cause the complex to be electrostatically neutral (¶ bridging pg 21-22).

Claim 33 has been excluded because 5% is not "8%" as newly amended.

Claims 35 and 41 are included because administering the complex to the skin/mucosa as taught by Behr inherently would activate APCs by toxin activation.

Cells would start expressing luciferase and this firefly "toxin" would be recognized as foreign by the animal, thereby activating APCs, including Langerhans cells.

Claim Rejections - 35 USC ' 103

5. Claims 23-33, 35, 37, 38, 40 and 41 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Behr (US Patent 6,013,240, Jan. 11, 2000) in view of Adachi (J. Virol., 1986, Vol. 59, pages 284-291) and Owada (Microbiol. Immunol. Feb. 1998, Vol. 242, No. 2, pg 97-107).

Parent application 60/058,933 (9-15-97) did not describe complexing DNA with a compound selected from the group consisting of sugars, PEI, PEI derivatives, or mixtures thereof (claim 23). Parent application 09/153,198 (9-15-98) described complexing DNA with PEI-mannose in a 5-10% glucose solution on pg 26, lines 1-9; therefore, claims 23-33, 35 and 37-42 have priority to 09/153,198 (9-15-98).

Behr taught a complex comprising i) PEI, and ii) plasmid DNA comprising a nucleic acid sequence encoding luciferase operatively linked to a promoter suspended in 5% glucose (col. 12, lines 53-57). Luciferase is an immunogenic protein because it is foreign to mammals and induces an immune response in mammals. Behr taught administering the complex to the skin or mucosa of an animal (claim 33, col. 6, lines 1-19). Behr taught the DNA could encode an HIV peptide (col. 3, lines 57-67). The phrase "transfecting antigen presenting cells" in the preamble does not bear patentable weight in considering the art because it may not occur. However, the method of Behr inherently results in transfecting APCs because dendritic cells (a type of antigen

presenting cell) are found in the epidermis (see definition of "dendritic cell", item 3). Case law established that reliance upon inherency in an obviousness rejection (103) instead of an anticipation rejection (102) is proper. In re Skoner, et al. 186 USPQ 80 (CCPA). Behr did not teach the HIV protein was derived from a reverse transcriptase dependent virus.

However, Adachi taught a plasmid encoding replication-defective HIV used for transfecting a wide array of eukaryotic cells (pg 284, col. 2, 8 lines from the bottom; pg 285, col. 1, Table 1; pg 289, Table 2).

Thus, it would have been obvious for one of ordinary skill in the art at the time the invention was made to administer a complex of a plasmid encoding an immunogenic protein and PEI in a glucose solution to the skin/mucosa of an animal to express the protein in cells of the animal as taught by Behr wherein the plasmid encoded HIV proteins as taught by Adachi. One of ordinary skill in the art would have been motivated to use PEI to administer the plasmid of Adachi because PEI increased transfection as compared to DNA alone (Behr, col. 8, lines 13-19; col. 13, lines 6-10). One of ordinary skill in the art would have been motivated to replace the plasmid encoding luciferase with the plasmid encoding HIV proteins to determine whether an immune response against the HIV antigens would occur *in vivo*. One of ordinary skill in the art at the time the invention was made would have been motivated to use PEI to deliver DNA encoding HIV proteins because it was well known in the art at the time of filing that PEI could be used to deliver DNA encoding HIV proteins to cells (Owada, see pg 98, "Cells and Virus", "Compounds").

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In this case, the desire to replace luciferase protein with an HIV protein was expressly taught by Behr. The desire to replace an HIV protein with a protein from replication-defective HIV would not require hindsight reasoning. One of ordinary skill in 1997 would have recognized that an attenuated HIV such as the replication-defective HIV of Adachi would prevent viral replication and death of the animal. One of ordinary skill in the art would have also recognized that attenuated HIV was desirable in a lab setting to add an extra measure of safety for lab technicians in case of accidental exposure.

Applicants argue Behr relates to using PEI for gene therapy but does not specifically provide the requirements needed to apply a plasmid to the skin or mucosa such that APCs are targeted and transfected (paragraph bridging pg 21-22 of response filed 6-7-04). Applicants' argument is not persuasive. The phrase "transfecting antigen presenting cells" in the preamble does not bear patentable weight in considering the art because it may not occur. The body of the claim does not require transfecting APCs. However, the method of Behr inherently results in transfecting APCs because dendritic

cells (a type of antigen presenting cell) are found in the epidermis (see definition of "dendritic cell", item 3). Methods of applying plasmids encoding antigens to the skin such that APCs were transfected were known in the art (see Carson, US Patent 5,679,647; col. 36-37, Examples 11-12). Therefore, one of ordinary skill in the art at the time of filing would have had a reasonable expectation of successfully taking the teachings of Behr and transfecting APCs of the skin.

Applicants argue Adachi adds nothing to the Behr reference. Adachi teaches the replication-defective HIV in claim 38.

Applicants argue Owada does not address using PEI for delivering genes. Applicants' argument is not persuasive. Owada need not teach all the limitations of the claims because Behr taught using PEI for delivering DNA encoding HIV antigens to the skin or mucosa *in vivo*. Owada provided additional motivation for one of ordinary skill in the art at the time the invention was made to use PEI to deliver DNA encoding HIV proteins because Owada used PEI to deliver DNA encoding HIV proteins *in vitro*.

In response to applicant's arguments against the references individually and "no linking teaching or guidance that would lead one of ordinary skill in the art to select the bits and pieces of the claimed invention from the voluminous options presented in the base reference" (pg 22, last 6 lines, of response filed 6-7-04), one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

6. Claims 23-33, 35 and 37-41 as newly amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over Behr (US Patent 6,013,240, Jan. 11, 2000) in view of Adachi (J. Virol., 1986, Vol. 59, pages 284-291) and Owada (Microbiol. Immunol. Feb. 1998, Vol. 242, No. 2, pg 97-107) as applied to claims 23-38, 40 and 41, further in view of Holler (US Patent 5,908,923).

The combined teachings of Behr, Adachi and Owada taught a complex comprising i) PEI, and ii) plasmid DNA comprising a nucleic acid sequence encoding a protein from replication-defective HIV operatively linked to a promoter suspended in 5% glucose (see 103 rejection above). The combined teachings of Behr, Adachi and Owada did not teach the protein from replication-defective HIV was from integrase defective HIV.

However, Holler taught a plasmid encoding replication-defective HIV that was integrase defective for use in vivo (col. 4, lines 51-54).

Thus, it would have been obvious for one of ordinary skill in the art at the time the invention was made to administer a complex of a plasmid encoding an HIV protein and PEI in a glucose solution to the skin/mucosa of an animal to express the protein in cells of the animal as taught by the combined teachings of Behr, Adachi and Owada wherein the plasmid encoding HIV proteins was integrase defective as taught by Holler. One of ordinary skill in the art would have been motivated to make the HIV integrase defective to prevent causing disease in the animal.

Applicants argue Holler merely teaches that the replication-defective, integrase-defective HIV is usable but does not say anything about the claimed method.

Applicants suggest Holler recommends that the gene can be successfully delivered by any method. However, the parent application (please refer to the instant application) cites Arthur and Song who both state only "low efficient" *in vitro* methods were known at the time. Applicants argument is not persuasive. Song taught APCs were successfully transfected with plasmid encoding HIV and that the APCs presented HIV antigens (pg 1946, col. 1, "Dendritic cell fraction contains antigen-presenting cells that can prime naïve T-cells in vitro"). Song taught administering retroviral particles encoding HIV IIIB env/rev to mice intramuscularly (pg 1943, col. 2, "Retroviral vectors" and "Immunizations...") or with dendritic cells transduced with the virus injected intraperitoneally (pg 1943, col. 2, "Retroviral vectors" and "Immunizations..."). Even if transfection efficiency was low (which has not been supported by applicants), the method of Song was a success. The teachings of Arthur have not been provided and are not of record. Holler provides a reasonable expectation of success because Holler transfected CEM (a lymphoblastoid cell line) with integrase-defective HIV. Therefore, one of ordinary skill in the art at the time the invention was made would still have a reasonable expectation of successfully transfecting APCs as claimed with the modification taught by Holler.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Double Patenting

The rejection of claims 23-33, 35, 37-41 of this application conflict with the claims of Application No. 08/989,301, now US Patent 6,130,089 has been withdrawn. The claims of '089 require increasing the concentration of dNTP in the cytosol of a recipient cell, which is not taught or suggested in the instant application or in combination with the art at the time of filing.

The following prior art remains of record but not relied upon because it is pertinent to applicant's disclosure:

The proceedings of the 3rd European conference on gene therapy of cancer, held from Sept. 11-13, 1997 at the University of Berlin, as supported by Diebold (Diebold et al., Advances in Experimental Med. and Biol., Oct. 1998, Vol. 451, pages 449-455). The preface of Advances in Experimental Med. and Biol., Oct. 1998, Vol. 451 (page v and vi) states that Vol. 451 contains the proceedings of the 3rd European conference on gene therapy of cancer. At the conference Diebold taught a complex comprising i) mannosylated PEI (PEI-man), and ii) plasmid DNA comprising a nucleic acid sequence encoding luciferase operatively linked to a promoter used to transfect dendritic cells via the mannose receptor (pg 452, line 10; pg 453, line 13-18). While Diebold described using a complex comprising PEI-man and DNA encoding an immunogenic protein at least a year and two days prior to the filing date of the instant application (Sept. 15, 1998), the conference was in Germany. 102(a) and (b) requires

that the information known in this country or published in this country or a foreign country prior. It does not appear that the information disclosed by Diebold was known in this country or published in any country until the publication of Advances in Experimental Med. and Biol., Vol. 451 in Oct. 1998. Therefore, the information disclosed by Diebold at the conference is not available under 102(a) or (b).

US Patent 6,420,176, application 09/153,198, claims a composition comprising DNA and mannosylated polyethylenimine, wherein said DNA encodes at least one immunogenic protein. The composition was restricted from the method of using in application 09/153,198.

Song (PNAS, March 1997, Vol. 94, pg 1943-1948) taught administering retroviral particles encoding HIV IIIB env/rev to mice intramuscularly (pg 1943, col. 2, "Retroviral vectors" and "Immunizations...") or with dendritic cells transduced with the virus injected intraperitoneally (pg 1943, col. 2, "Retroviral vectors" and "Immunizations...").

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER

dendritic cell

1. Follicular dendritic cells, found in germinal centres of spleen and lymph nodes, retain antigen for long periods.

2. Accessory (antigen presenting) cells, positive for Class II histocompatibility antigens, found in the red and white pulp of the spleen and lymph node cortex and associated with stimulating T-cell proliferation.

3. T lymphocyte found in epidermis and other epithelial cells involved in antigen recognition expressing predominantly __TCR receptors (dendritic epidermal cells: DECs). (4) Dopa positive cells derived from neural crest and found in the basal part of epidermis.

(13 Nov 1997)

Previous: dendrites, dendritic, dendritical, dendritic calculus, dendritic cataract
Next: dendritic cells, dendritic corneal ulcer, dendritic depolarisation

Notice of References Cited	Application/Control No. 10/081,922	Applicant(s)/Patent Under Reexamination LISZIEWICZ ET AL.	
	Examiner Michael C. Wilson	Art Unit 1632	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-			
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NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	On-line medical dictionary definition of "dendritic cell"
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.